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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/049,393	08/28/2002	Antonius Helena Adolf Bom	0-1999.475 US	3834

7590 12/31/2003

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EXAMINER	
MAIER, LEIGH C	

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 12/31/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/049,393	BOM ET AL.	
	Examiner	Art Unit	
	Leigh C. Maier	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *7-19* is/are pending in the application.

4a) Of the above claim(s) *7-10 and 15-19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *11-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *2*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claim 7, drawn to cyclophane compounds, classified in class 540, various subclasses, depending on the cyclophane.

II. Claims 8-10, drawn to a kit comprising a neuromuscular blocking agent and a chelator, classified in class 514, various subclasses, depending on the particular agents.

III. Claims 11-14, drawn to a method for reversal of neuromuscular block, classified in class 514, various subclasses, depending on the particular agent.

IV. Claims 15-19, drawn to a pharmaceutical composition comprising a chemical chelator, classified in class 514, various subclasses, depending on the particular chelator.

Inventions I and III are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, it is the former. The product is a cyclophane, a class of chelator. The method can be practiced employing another type of chelator.

Inventions I, II, and IV are all products. Invention I is a genus of cyclophanes that may be used to prepare the compositions of II and IV. However, these compositions may also be prepared with materially different compounds, such as cyclodextrins.

Inventions IV and III are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, it is the latter. The product, a pharmaceutical composition comprising a chemical chelator, can be used for drug delivery, as admitted by Applicant. See specification at page 5, lines 21-22.

Inventions II and III are not related. In both cases, the kit and pharmaceutical composition, respectively, the product may contain a cyclophane compound, but may also be prepared with materially different compounds, as discussed above. Also, the components in addition to the chelator are not the same in the two products.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

Because these inventions are distinct for the reasons given above and the search required for the groups are not coextensive, restriction for examination purposes as indicated is proper. The search for a method would not be the same as that for a composition. The instant compositions would in turn require a search not required for a compound.

This application contains claims directed to the following patentably distinct species of chemical chelators.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species (family) of chelator for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, 8, 9, 11, 12, are 15 are generic. Claims 13 and 16 are sub-generic. Claims 7 and 19 are specific to cyclophanes. Claims 10, 14, 17, and 18 are specific to cyclodextrins.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

During a telephone conversation with Mark Milstead on November 14, 2003 a provisional election was made with traverse to prosecute the invention of Group IV, claim11-14 with cyclodextrins being the elected chelator. Affirmation of this election must be made by applicant in replying to this Office action. Claims 7-10 and 15-19 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 11-13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the neuromuscular block drugs recited in claim 12 using γ–cyclodextrins, does not reasonably provide enablement for all NB drugs with all cyclodextrins (CDs). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

With regard to other NB drugs, DÉSIRÉ (Experientia, 1987) teaches that the neuromuscular blocking effect of sarin and soman may be reversed by the use of β–cyclodextin. It is known that CD complexation depends roughly on the relative size of the compound to be complexed and the cavity size of the particular CD (α–, β–, or γ–). However, the reference teaches that the effect of tabun is not reversed even though the structure of tabun is very similar to sarin. Therefore, the art could not be considered very predictable.

With regard to the use of all CDs, in a post-filing publication, BOM (Angew. Chem. Int. Ed., 2002) teaches that "[o]nly γ–cyclodextrin, with the largest cavity size . . . showed reasonable reversal activity *in vitro* against rocuronium . . ." See page 266, right column, second full paragraph. Further, Table I of the instant specification tabulates data for a number of NB drugs and CDs. Examination of the data leads to the conclusion that only the γ–cyclodextrins would have reasonable activity for the reversal of the NB action of the recited drugs.

In light of the forgoing, it is concluded that one of ordinary skill would require undue experimentation at great expense in order to practice the invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 11 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over DÉSIRÉ et al (Experientia, 1987).

DÉSIRÉ teaches that sarin and soman are inactivated by cyclodextrins in vitro. The reference does not specifically exemplify actual administration of a CD to a subject. However, the reference expressly suggests such administration. See abstract.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to administer a CD to a subject to reverse the neuromuscular effect induced by sarin or soman. One of ordinary skill would be motivated to employ a CD for this method and reasonably expect success thereof based on the teaching of DÉSIRÉ.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground

provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 11-14 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 9 of U.S. Patent No. 6,670,340. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of '340 recites a more narrowly drawn method for reversing neuromuscular block using mercaptocyclodextrins. The instant method using a broader set of CDs would be anticipated by the method recited in '340.

Allowable Subject Matter

DÉSIRÉ teaches as set forth above. The teaching is limited specifically to phosphonofluoridates. The reference does not teach or fairly suggest the instant method wherein the NB agents are those recited in claim 12. Claims 12 and 14 appear to be free of the art but subject to other rejections set forth above.

Examiner's hours, phone & fax numbers

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leigh Maier whose telephone number is (703) 308-4525. The examiner can normally be reached on Monday-Friday 7:00 to 3:30 (ET).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson (703) 308-4624, may be contacted. The fax number for Group 1600, Art Unit 1623 is (703) 308-4556 or 305-3592.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-1235.
Visit the U.S. PTO's site on the World Wide Web at http://**www.uspto.gov**. This site contains lots of valuable information including the latest PTO fees, downloadable forms, basic search capabilities and much more.

Leigh C. Maier
Patent Examiner
December 29, 2003